Peritoneal mesothelioma

Introduction

Peritoneal disease accounts for just under a third of all malignant mesothelioma. Its insidious onset means that diagnosis is often made at an advanced stage, however, new therapeutic techniques are starting to lead to improved outcomes.

Discussion

Epidemiology

Malignant mesothelioma is an aggressive tumour of serosal surfaces. It is most commonly seen in the pleura (70%), but peritoneal disease represents 20–30% of all cases. Other rare sites include pericardium and the tunica vaginalis of the testis (Bridda et al, 2007).

Malignant mesothelioma remains a rare condition but its incidence is still rising following widespread use of asbestos in the industrial period of the 20th century. It is estimated that the incidence will peak in Europe in 2015–2020 (Robinson and Lake, 2005).

The association between asbestos exposure and peritoneal disease is less strong than in the case of pleural mesothelioma, with only 50% of patients with peritoneal mesothelioma having a history of asbestos exposure, as opposed to 80% in pleural disease (Bridda et al, 2007).

Pathogenesis

The asbestos fibres appear to exert carcinogenic effects via several different routes. Persistent irritation of the peritoneum leads to chronic inflammation with repeated cycles of damage and repair to mesothelial cells. This leads to a release of cytokines and reactive oxygen species with a subsequent risk of DNA damage. The fibres also directly interfere with the mitotic process by disruption of mitotic spindles, with the potential to lead to aneuploidy and other forms of chromosomal damage that characterize mesothelioma (Ault et al, 1995).

Dr James Berrill *is Specialist Registrar in Gastroenterology, University Hospital of Llandough, Cardiff CF64 2XX,*
Dr Hasan Haboubi *is Senior House Officer in Medicine and* **Dr Paul Duane** *is Consultant Gastroenterologist, Morriston Hospital, Swansea*

Correspondence to: Dr J Berrill

Clinical features

The latent period between asbestos exposure and onset of peritoneal mesothelioma is usually around 20–30 years (Bridda et al, 2007). The most common presentations are abdominal distension as a result of ascites, abdominal pain, or occasionally in more advanced illness bowel obstruction. Other constitutional symptoms such as anorexia, fatigue and weight loss are often present.

Diagnosis

Routine blood tests may show non-specific features of malignancy with anaemia, raised erythrocyte sedimentation rate and hypoalbuminaemia. Serum tumour markers are not currently used in the diagnosis, but research is ongoing into serum mesothelin-related protein as a potential marker for malignant mesothelioma (Robinson et al, 2003). CA-125 levels are often raised in pathology of the peritoneal surfaces, in addition to ovarian cancer, but it lacks sufficient specificity to be used alone in the diagnosis of peritoneal mesothelioma.

Diagnosis can be made using cytological analysis of either ascitic fluid or fine-needle aspirate of the tumour. A tumour biopsy may be needed and immunohistochemistry is used to distinguish if the

Figure 1. Calcified pleural plaques suggesting previous asbestos exposure.

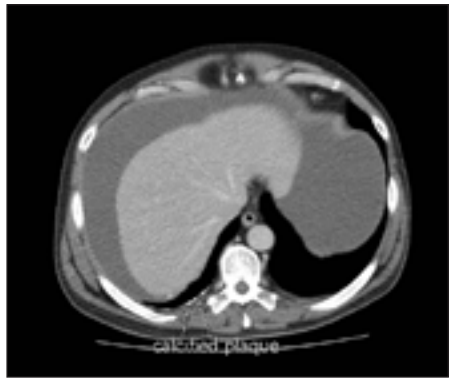
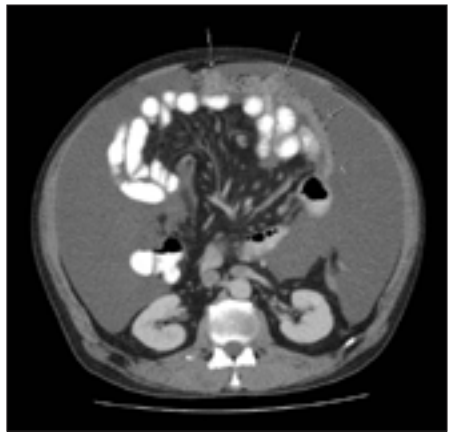


Figure 2. Computed tomography scan showing extensive ascites with a sizeable omental mass.



Case Report

A 59-year-old building surveyor presented with a 2-month history of lethargy and abdominal swelling. There was no associated abdominal pain, change in bowel habit or jaundice. There was no significant past medical history. His alcohol intake was approximately 60 units per week.

Examination revealed gross ascites, but no palpable masses, lymphadenopathy or stigmata of chronic liver disease. Blood tests revealed a microcytic anaemia (haemoglobin 9.3 g/dl, mean corpuscular volume 72.5 fl). Other abnormalities were high platelets (740 x10^9/litre), raised erythrocyte sedimentation rate (101 mm/hr) and low albumin (30 g/litre). Other laboratory investigations were normal.

Computed tomography scan revealed calcified pleural plaques suggesting previous asbestos exposure (*Figure 1*) and extensive ascites with a sizeable omental mass (*Figure 2*).

Diagnostic tap of the ascitic fluid showed atypical mesothelial cells suspicious of malignancy (*Figure 3*). An omental biopsy was performed, and immunohistochemistry showed positive staining for calretinin (*Figure 4a*) and thrombomodulin (*Figure 4b*), and negative for carcinoembryonic antigen (CEA) (*Figure 4c*) and BerEP4 (*Figure 4d*). A diagnosis of malignant mesothelioma was made.

On further questioning regarding his occupational asbestos exposure he admitted to 'throwing it around like snowballs'. His ascites was drained for symptomatic benefit, and after an oncology review he proceeded to a course of chemotherapy.

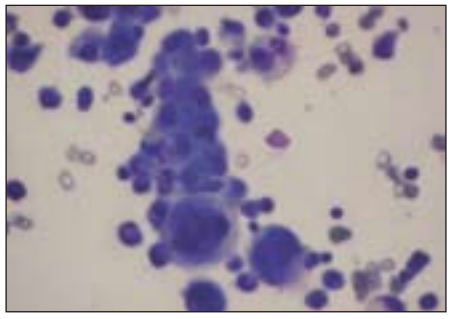


Figure 3. Large atypical mesothelial cells.

tumour is mesothelial in origin and whether it is malignant (Robinson et al, 2003; Hassan et al, 2006).

Computed tomography scanning is the method of choice for imaging peritoneal mesothelioma. Thickening and tumour nodules of the peritoneum, mesentery and omentum can be seen, in addition to ascites. Its diffuse spread makes accurate tumour measurements difficult (Hassan et al, 2006).

Management

Diffuse malignant peritoneal mesothelioma has usually been regarded as a terminal condition, with treatment consisting of systemic chemotherapy and palliative surgery, and median survival approximately 1 year (Hassan et al, 2006).

However, several specialist centres have studied more aggressive treatment plans consisting of cytoreductive surgery and perioperative intraperitoneal chemotherapy, and these have shown remarkable improvements in survival with a significant proportion of patients alive at 5 years (Sugarbaker, 2003; Sugarbaker et al, 2006). Cytoreductive surgery involves the removal of all visible tumours on the surface of any viscera and the total removal of the diseased peritoneum. On completion of surgery hyperthermic intraperitoneal chemotherapy is performed with the aim of treating any residual tumour cells.

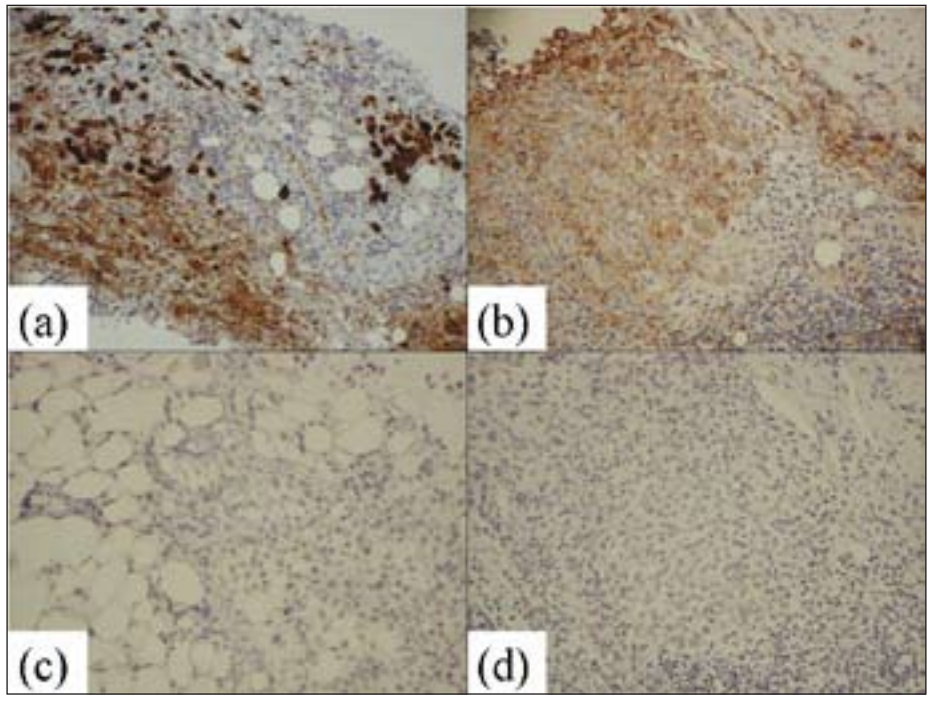


Figure 4. Immunohistochemistry stains: positive for (a) calretinin and (b) thrombomodulin, and negative for (c) carcinoembryonic antigen and (d) BerEP4, differentiating mesothelioma from adenocarcinoma.

This evolvement of treatment approaches in the last decade has shown that a marked increase in survival may be possible in patients who were previously considered to have terminal disease.

Conclusions

The incidence of peritoneal mesothelioma will continue to rise over the next few years, so clinicians need to be aware of its diagnosis and also of the broadening therapeutic options that are available. BJHM

Ault JG, Cole RW, Jensen CG, Jensen LC, Bachert

LA, Rieder CL (1995) Behavior of crocidolite asbestos during mitosis in living vertebrate lung epithelial cells. *Cancer Res* **55**(4): 792–8

Bridda A, Padoan I, Mencarelli R, Frego M (2007) Peritoneal mesothelioma: a review. *Med Gen Med* **9**(2): 32

Hassan R, Alexander R, Antman K et al (2006) Current treatment options and biology of peritoneal mesothelioma: meeting summary of the first NIH peritoneal mesothelioma conference. *Ann Oncol* **17**(11): 1615–19

Robinson BW, Lake RA (2005) Advances in malignant mesothelioma. *N Engl J Med* **353**(15): 1591–603

Robinson B, Creaney J, Lake R et al (2003) Mesothelin-family proteins and diagnosis of mesothelioma. *Lancet* **362**(9396): 1612–16

Sugarbaker PH (2003) Management of peritoneal surface malignancy. *Surg Oncol Clin N Am* **12**(3): 21–4

Sugarbaker PH, Yan TD, Stuart OA, Yoo D (2006) Comprehensive management of diffuse malignant peritoneal mesothelioma. *Eur J Surg Oncol* **32**(6): 686–91